Obesità: fenotipizzazione e risvolti terapeutici

LA CHIRURGIA BARIATRICA

ALMA MATER STUDIORUM
UNIVERSITÀ DI BOLOGNA

Paolo Bernante

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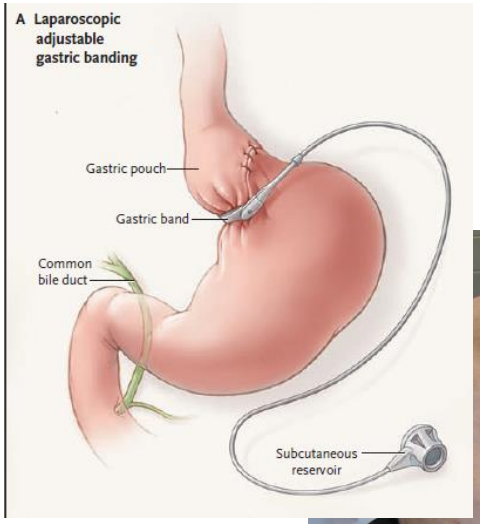
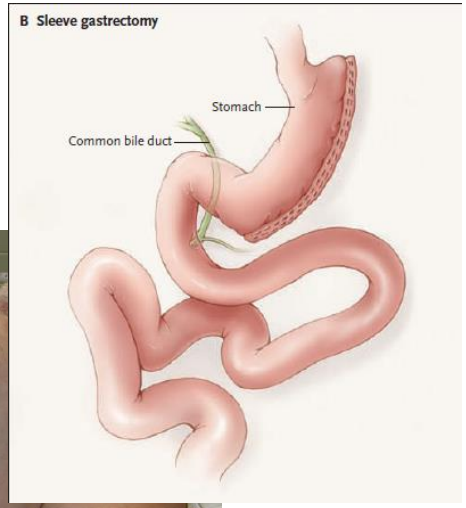
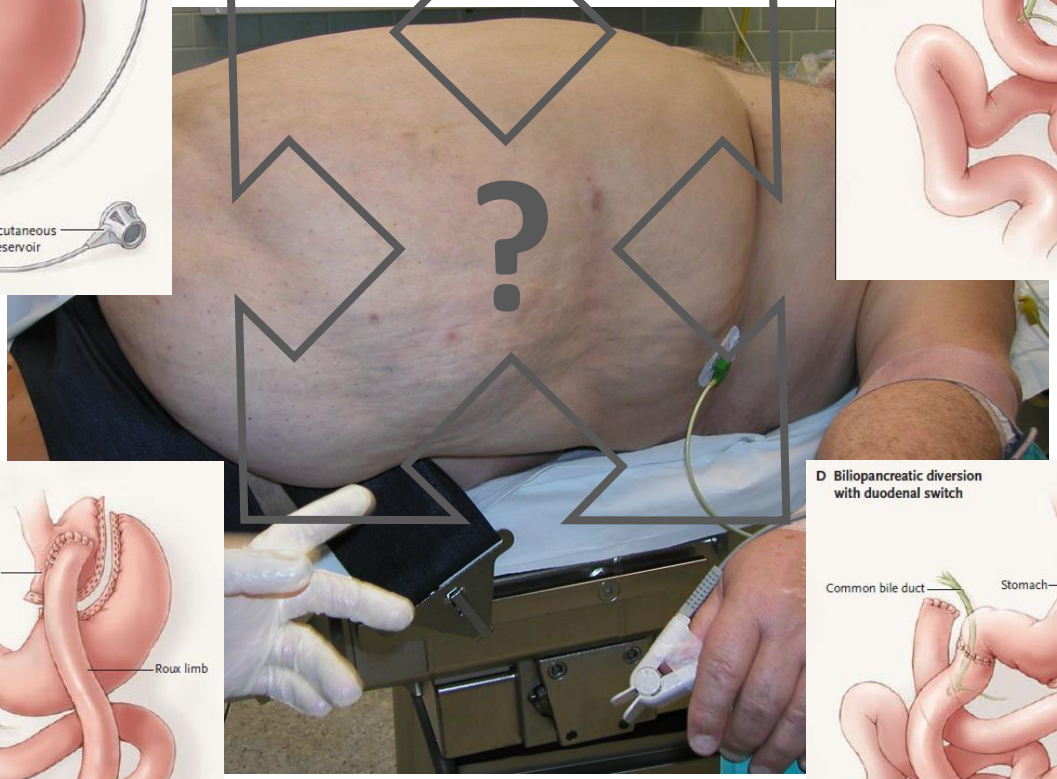
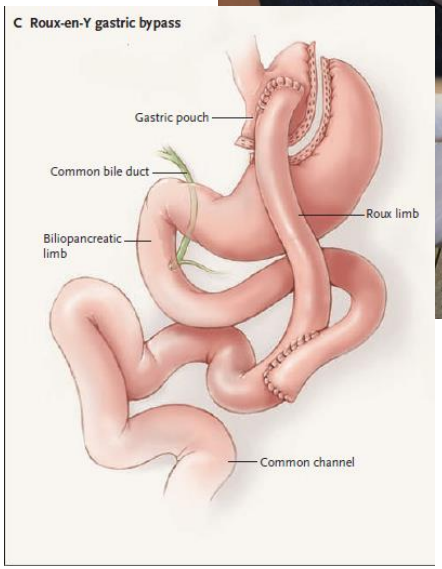
IRCCS Policlinico di Sant'Orsola

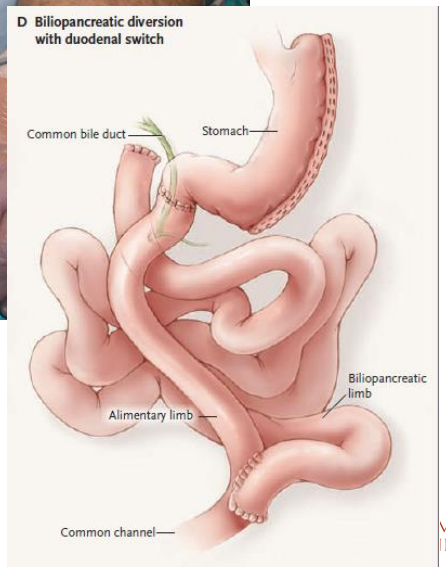
UNICO PROBLEMA, MOLTE SOLUZIONI: PERCHE'?











Precision Medicine for Obesity

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Andres Acosta, MD, PhD[1]

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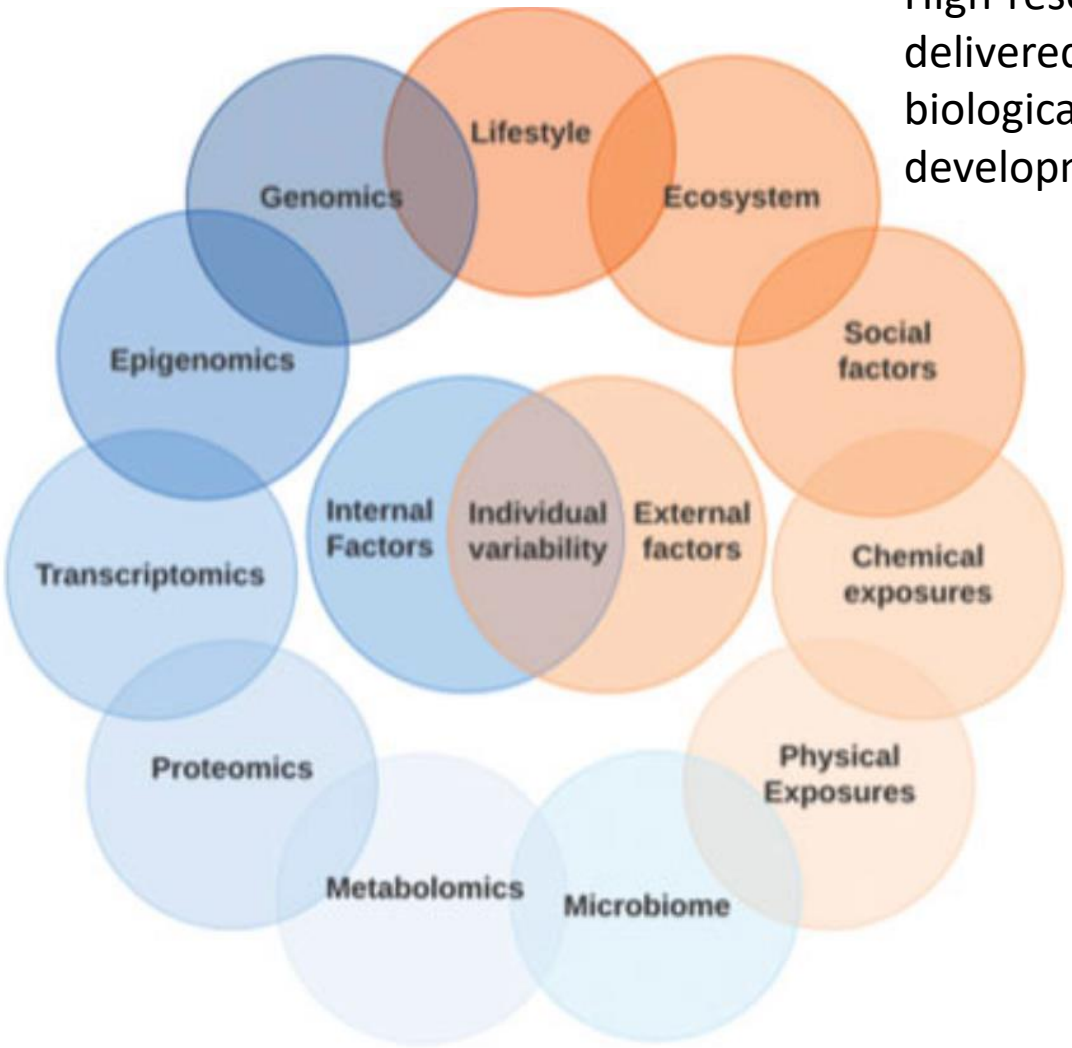
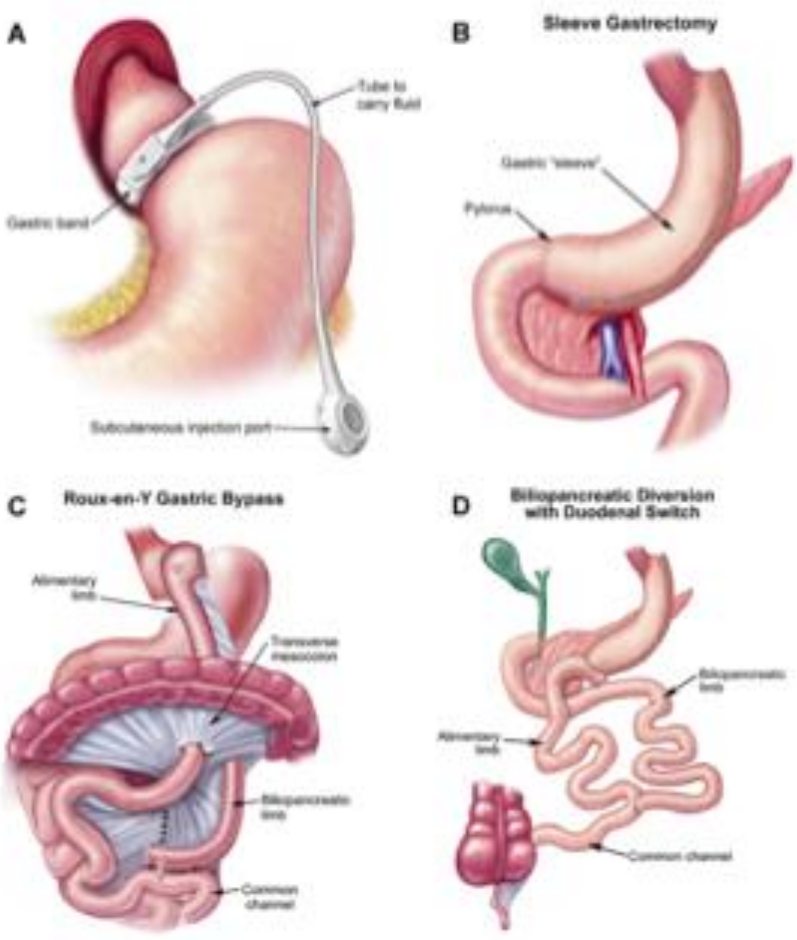
Dig Dis Interv 2021;5:239–248.



High-resolution biotechnologies have so far delivered information about a myriad of biological variants that contribute to obesity development.

RESTRIZIONE E MALASSORBIMENTO



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 AUGUST 23, 2007 VOL. 357 NO. 8

Effects of Bariatric Surgery on Mortality in Swedish Obese Subjects

Lars Sjöström, M.D., Ph.D., Kristina Narbro, Ph.D., C. David Sjöström, M.D., Ph.D., Kristjan Karason, M.D., Ph.D., Bo Larsson, M.D., Ph.D., Hans Wedel, Ph.D., Ted Lystig, Ph.D., Marianne Sullivan, Ph.D., Claude Bouchard, Ph.D., Björn Carlsson, M.D., Ph.D., Calle Bengtsson, M.D., Ph.D., Sven Dahlgren, M.D., Ph.D., Anders Gummesson, M.D., Peter Jacobson, M.D., Ph.D., Jan Karlsson, Ph.D., Anna-Karin Lindroos, Ph.D., Hans Lönroth, M.D., Ph.D., Ingmar Näslund, M.D., Ph.D., Torsten Olbers, M.D., Ph.D., Kaj Stenlöf, M.D., Ph.D., Jarl Torgerson, M.D., Ph.D., Göran Ågren, M.D., and Lena M.S. Carlsson, M.D., Ph.D., for the Swedish Obese Subjects Study

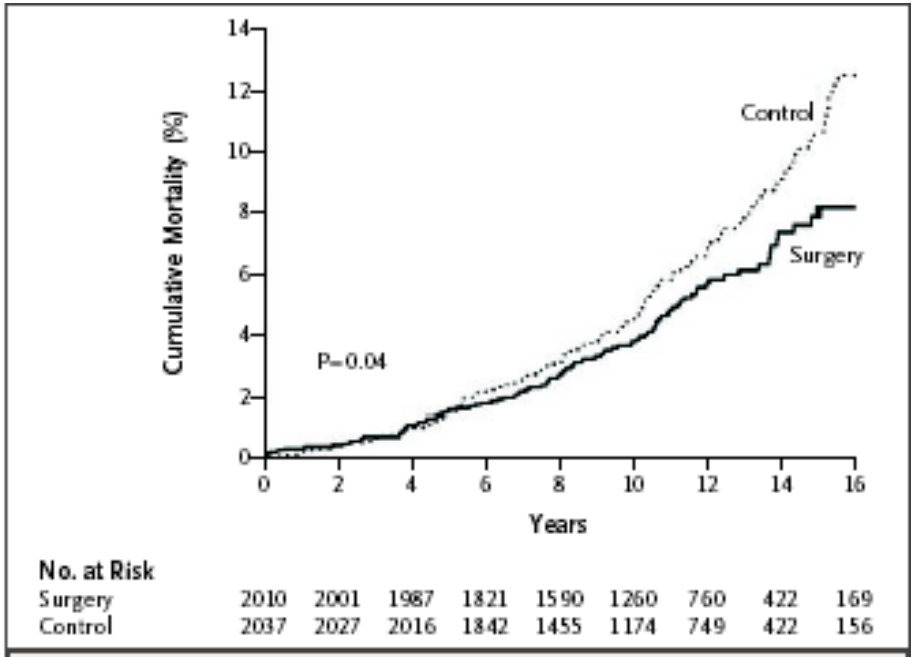


Figure 2. Unadjusted Cumulative Mortality.

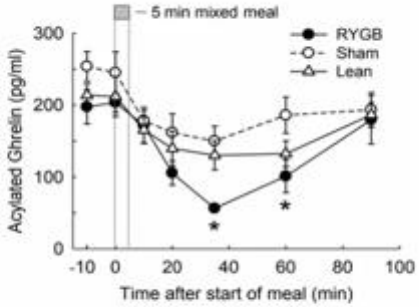
The hazard ratio for subjects who underwent bariatric surgery, as compared with control subjects, was 0.76 (95% confidence interval, 0.59 to 0.99; P= 0.04), with 129 deaths in the control group and 101 in the surgery group.

Metabolic surgery *is associated with the reorientation of the levels of* ***multiple hormones***

Table 5.2 Characteristics of entero-hormones after bariatric operations

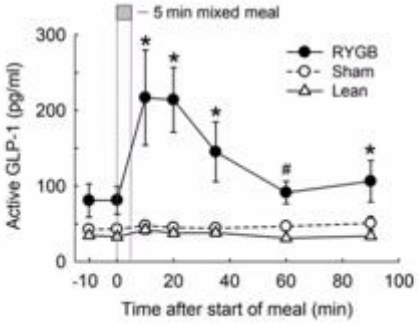
	Origin	Satiety	Glycemic control	GI motility	RYGB	LSG	LAGB	BPD	BPD-DS
GLP-1	L cells	↑	↑	↓	↑	↑	No Δ(delta)	↑	↑
GIP	K cells	No Δ(delta)	↑	No Δ(delta)	↓	Unknown	No Δ(delta)	↓	↓
PYY	L cells	↑	↑ or no Δ(delta)	↓	↑	↑ or no Δ(delta)	No Δ(delta)	↑	↑
Oxyntomodulin	L cells	↑	↑	↓	↑	↑	No Δ(delta)	↑	↑
CCK	I cells	↑	No Δ	↑	?	↑ or no Δ(delta)	Unknown	Unknown	Unknown
Ghrelin	Oxyntic	↓	No Δ	No Δ	↓	↓↓	No Δ(delta)	No Δ(delta)	↓↓

Ghrelin

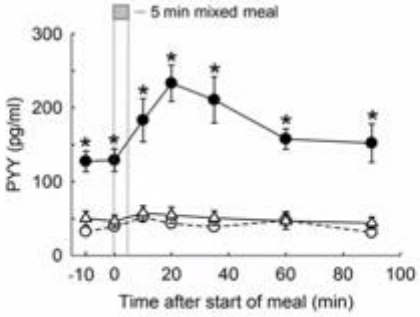


MBS has paved the way for more effective drugs

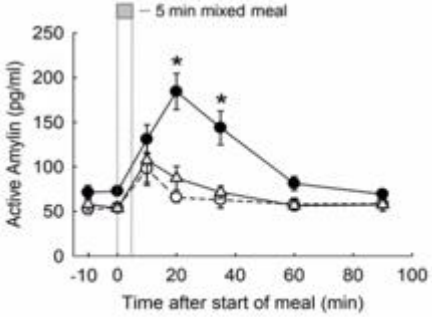
GLP-1



PYY



Amylin



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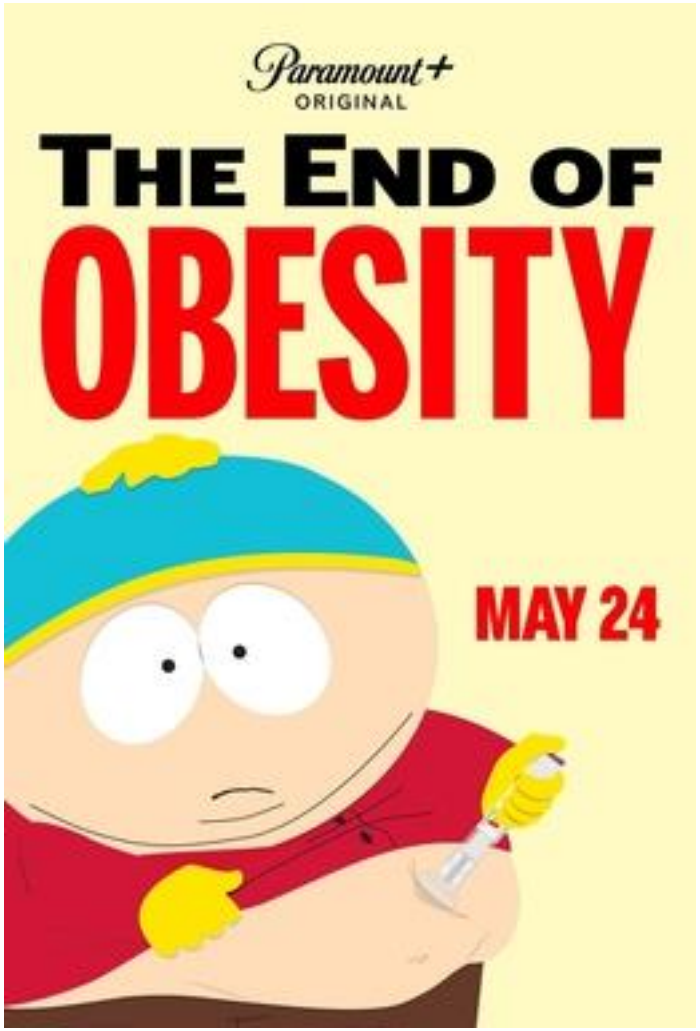
SOUTH PARK



and the end of bariatric surgery too???

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Anti-obesity drug discovery: advances and challenges

Timo D. Müller[1,2]✉, *Matthias Blüher*[3], *Matthias H. Tschöp*[4,5] *and Richard D. DiMarchi*[6]✉

NATURE REVIEWS | DRUG DISCOVERY VOLUME 21 | MARCH 2022

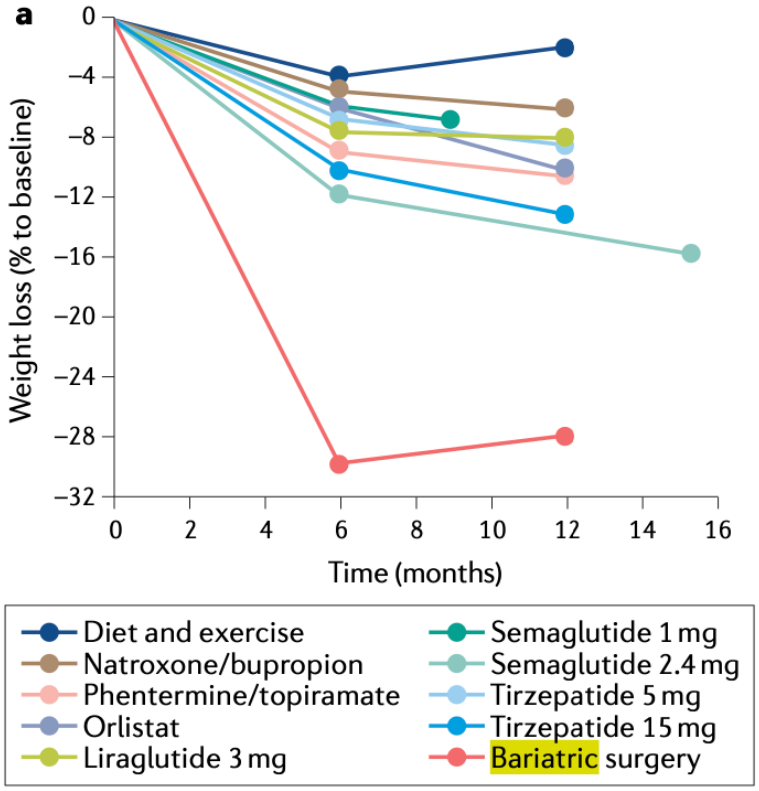

Fig. 3 | **Body weight loss by AOMs in humans and rodents.** I
currently approved anti-obesity medications (AOMs) and bari
body weight loss in rodents and humans (part **b**). Data in pane
bupropion[292], phentermine/topiramate[291], semaglutide 1 mg (I
15 mg)[126]. Data in panel **b** refer to naltrexone/bupropion[39,295], c
phentermine[121,145], semaglutide[38,123] and tirzepatide[122,127].

ELSEVIER

Surgery for Obesity and Related Diseases 20 (2024) 425–431

SURGERY FOR OBESITY AND RELATED DISEASES

ASMBS Guidelines/Statements

American Society for Metabolic and Bariatric Surgery 2022 estimate of metabolic and bariatric procedures performed in the United States

Benjamin Clapp, M.D., F.A.S.M.B.S.[a,*], Jaime Ponce, M.D., F.A.S.M.B.S.[b], John Corbett, M.D.[c], Omar M. Ghanem, M.D., F.A.S.M.B.S.[d], Marina Kurian, M.D., F.A.S.M.B.S.[e], Ann M. Rogers, M.D., F.A.S.M.B.S.[f], Richard M. Peterson, M.D., F.A.S.M.B.S.[g], Teresa LaMasters, M.D., F.A.S.M.B.S.[h], Wayne J. English, M.D., F.A.S.M.B.S.[i]

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Received 15 January 2024; accepted 21 January 2024

Abstract

Background: Metabolic and bariatric surgery (MBS), despite being the most effective durable treatment for obesity, remains underused as approximately 1% of all qualified patients undergo surgery. The American Society for Metabolic and Bariatric Surgery established a Numbers Taskforce to specify the annual rate of obesity treatment interventions utilization and to determine if patients in need are receiving appropriate treatment.
Objective: To provide the best estimated number of metabolic and bariatric procedures being performed in the United States in 2022.
Setting: United States.
Methods: We reviewed data from the Metabolic and Bariatric Surgery Accreditation and Quality Improvement Program and National Surgical Quality Improvement Program. In addition, data from industry and state databases were used to estimate activity at non-accredited centers. Data from 2022 were compared mainly with data from the previous 2 years.
Results: Compared with 2021, the total number of MBS performed in 2022 increased from approximately 262,893 to 280,000. The sleeve gastrectomy (SG) continues to be the most commonly performed procedure. The gastric bypass procedure trend remained relatively stable. The percentage of revision procedures and biliopancreatic diversion with duodenal switch procedures increased

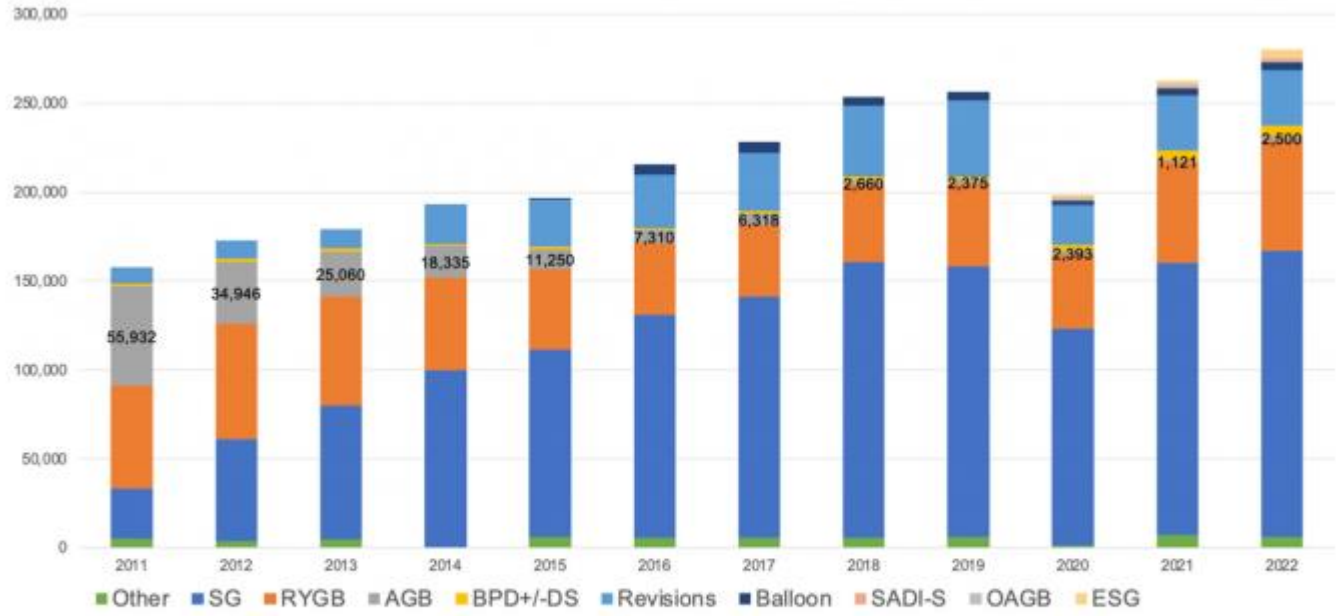
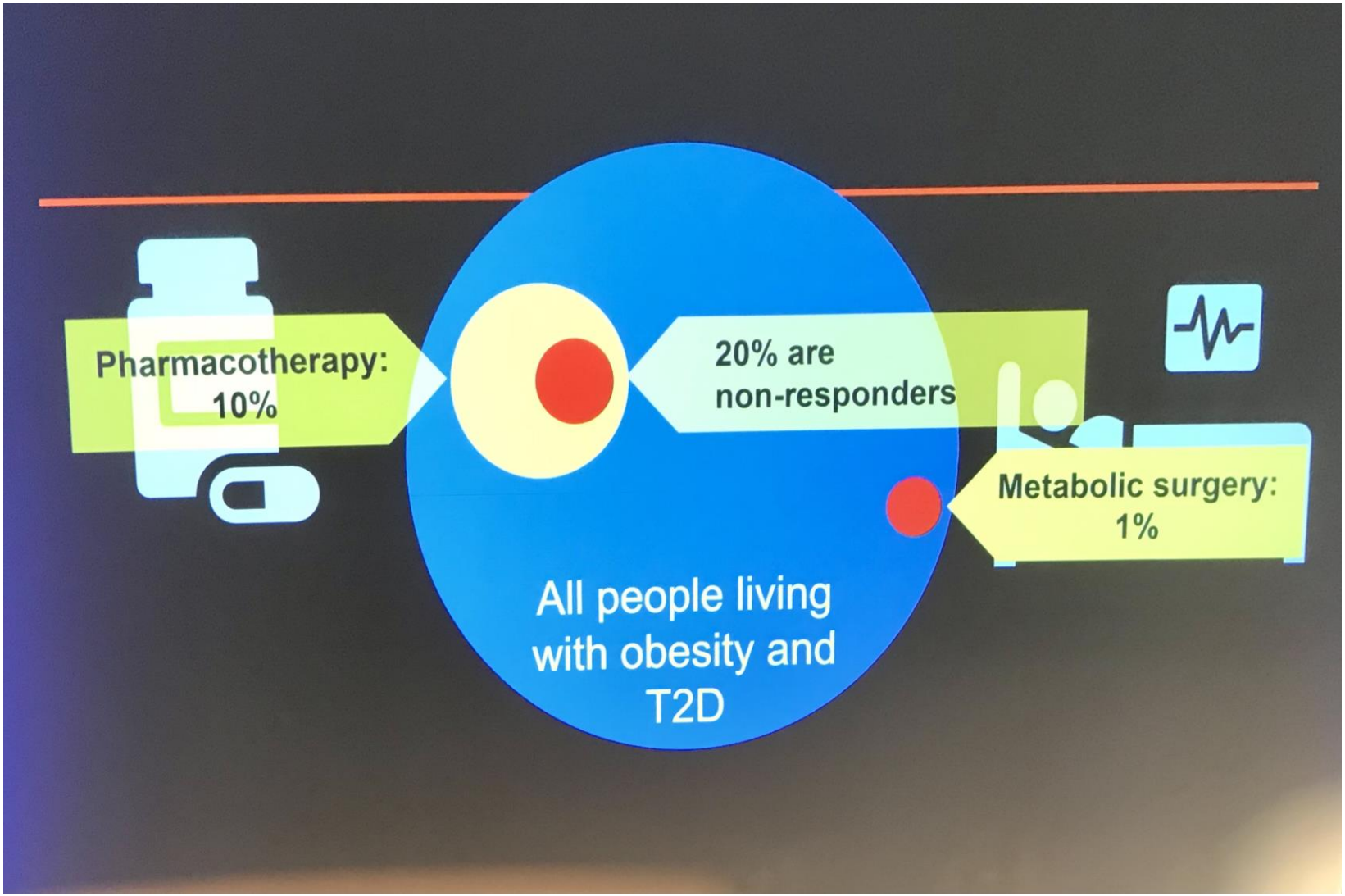


Fig. 1. Metabolic and bariatric surgery procedure trends: 2011–2022. AGB = adjustable gastric band; BPD-DS = biliopancreatic diversion with duodenal switch; ESG = endoscopic sleeve gastroplasty; OAGB = one-anastomosis gastric bypass; RYGB = Roux-en-Y gastric bypass; SADI-S = single-anastomosis duodeno-ileostomy with sleeve; SG = sleeve gastrectomy.

The impact of the new GLP1-RA has not been demonstrated yet in the 2022 data but ***is expected to drop the number of bariatric cases****. This will likely be demonstrated in 2 years with the next Task Force report*



by Carel le Roux (University College Dublin, Ireland)

	TIPOLOGIA DI INTERVENTO		
21	Si suggerisce, nel caso di trattamento chirurgico del diabete, di preferire nei pazienti con obesità di classe I (BMI tra 30 e 34.9 Kg/m^2) e DM2 non controllato interventi di RYGB, LABG o SG. Altri interventi, quali OAGB e BPD, sono ugualmente indicati sulla base di evidenze indirette.	Debole a favore	Molto bassa
22	Si raccomanda, nel caso di trattamento chirurgico del diabete, di preferire nei pazienti con obesità di classe ≥ II (BMI ≥35 Kg/m^2) e DM2 non controllato, interventi di RYGB anche funzionale e OAGB e sue varianti. Altri interventi, quali SG, LABG, BPD, BPD-DS, SADI-S, SAGI, BPBI e plicatura gastrica (GCP) sono ugualmente indicati sulla base di evidenze indirette.	Forte a favore	Alta
23	Non ci sono evidenze che consentano di preferire un intervento di chirurgica metabolico-bariatrica per il trattamento dell'obesità di classe I (BMI tra 30 e 34.9 Kg/m2) ed almeno una comorbidità non controllata.	Debole né a favore né contro	Molto bassa

24	Si raccomanda, nel caso di trattamento chirurgico dell'obesità, di preferire nei pazienti con obesità di classe ≥ II (BMI ≥35 Kg/m^2) ed almeno una comorbidità, interventi di RYGB anche funzionali, DS e BPD. Altri interventi, quali OAGB e sue varianti, SADI-S, SAGI, SG,	Debole a favore	Moderata
	VGB, BPBI, LAGB sono ugualmente indicati seppur siano disponibili meno evidenze di efficacia sugli outcome critici. Interventi di GCP sono da considerarsi solo in caso in cui la sicurezza sia prioritaria, rispetto all'efficacia.		
25	Si suggerisce, nel caso di trattamento chirurgico dell'obesità, di preferire nei pazienti con obesità di classe III (BMI ≥40 kg/m^2), interventi maggiormente efficaci sul peso corporeo (DS, RYGB anche funzionali, BPD, OAGB e sue varianti, SAGI, BPBI, VGB, LAGB e SG) e di riservare quelli meno efficaci, ma meno invasivi (GCP) a pazienti con maggiori fragilità.	Debole a favore	Molto bassa
ENDOSCOPIA BARIATRICA PRIMARIA			
26	Si suggerisce l'impiego della endoscopia bariatrica primaria nei pazienti con BMI≥ 30 Kg/m2, per il trattamento dell'obesità.	Debole a favore	Bassa

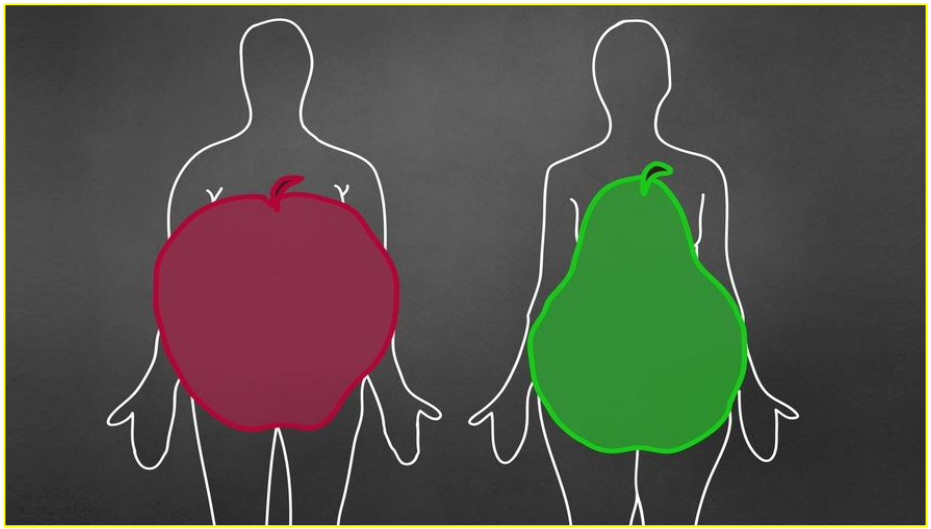
OBESITY PHENOTYPES

Table 1 Summary of defining criteria of different obesity phenotypes

	Underweight	MHNW	MUNW	MHO	MUO	SO
Waist circumference	normal	normal	Normal/high	normal	high	High WC and/or BMI>25
BMI (kg/m^2)	<18.5	18.5 – 24.9	18.5 – 24.9	>25	>25	
Visceral adipose tissue	Low	Low	High fat mass	Low	High	High fat mass
Lean mass	–	–	–	High	–	Low
Metabolic abnormalities	–	Absent	Present	Absent	Present	Present

Normal values are in green, pathological ones are in red, and the intermediate ones in orange. Waist circumference categorized as normal (men < 102 cm and women < 88 cm) or high (men ≥ 102 cm and women ≥ 88 cm). Visceral adipose tissue and lean mass are a non-standardized measure actually. Metabolic abnormalities refer to the metabolic syndrome defining criteria

BMI body mass index, *MHNW* metabolically healthy normal weight, *MUNW* metabolically unhealthy normal weight, *MHO* metabolically healthy overweight/obese, *MUO* metabolically unhealthy overweight/obese, *SO* sarcopenic obese



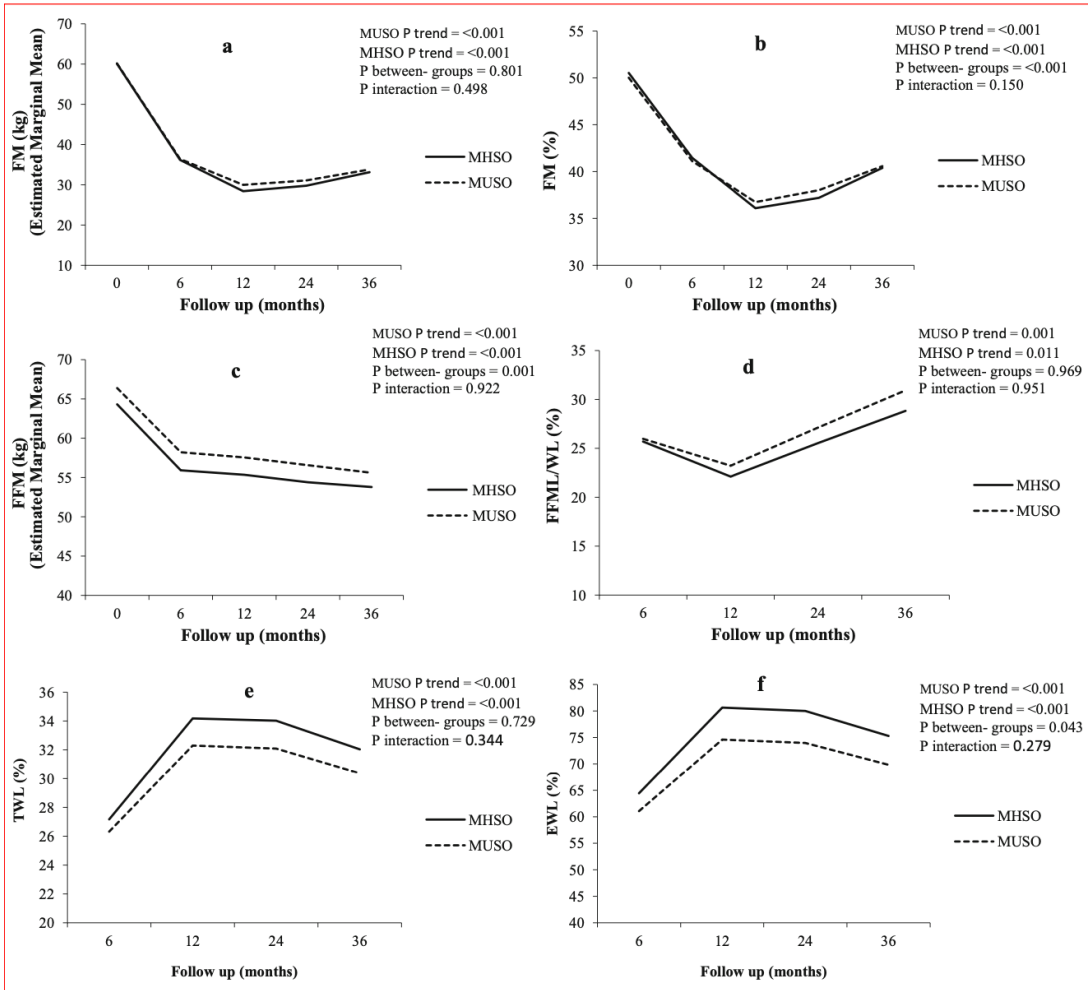


Fig. 1 Trend of different characteristics of MHSO and MUSO individuals during 36 months of follow-up. **a** Fat mass (FM, kg). **b** Fat mass percent (FM%). **c** Fat-free mass (FFM, kg). **d** Fat-free mass loss/weight loss% (FFML/WL%). **e** Total weight loss (TWL%). **f** Excess weight loss (EWL%)

World J Surg (2023) 47:209–216
https://doi.org/10.1007/s00268-022-06769-6

World Journal of Surgery

ORIGINAL SCIENTIFIC REPORT

Comparing Effects of Bariatric Surgery on Body Composition Changes in Metabolically Healthy and Metabolically Unhealthy Severely Obese Patients: Tehran Obesity Treatment Study (TOTS)

Minoo Heidari Almasi[1] · Maryam Barzin[1] · Maryam Mahdavi[1] · Alireza Khalaj[2] · Danial Ebrahimi[3] · Majid Valizadeh[1] · Farhad Hosseinpanah[1]

Accepted: 10 September 2022 / Published online: 2 October 2022

Conclusion Despite a lower decrease of FFML/WL% and a greater increase in TWL and EWL in MHSO phenotype at some time points, there were no clinically significant differences between the study groups in terms of body composition changes throughout the follow-up period.

OBESITY PHENOTYPES

- **Current obesity classifications** based on BMI, abnormal waist circumference, metabolically abnormal obesity, or the obesity staging system identify cardiometabolic disease and mortality risk. However, these severity-based classifications or staging systems **predominantly address cardiometabolic risk** and do not address patho-physiological or etiological heterogeneity of obesity.

- There is a critical need to develop a valid classification of obesity based on pathogenesis and to ascertain its utility in obesity management to improve outcomes In fact, the National Institutes of Health (NIH) has recognized the need to identify **predictors of response to obesity treatment** as a key approach to successfully manage this epidemic.

Original Article
CLINICAL TRIALS AND INVESTIGATIONS

Obesity

Selection of Antiobesity Medications Based on Phenotypes Enhances Weight Loss: A Pragmatic Trial in an Obesity Clinic

Andres Acosta [1], Michael Camilleri [1], Barham Abu Dayyeh[1], Gerardo Calderon[1], Daniel Gonzalez[1], Alison McRae[1], William Rossini[1], Sneha Singh[1], Duane Burton[1], and Matthew M. Clark[2]

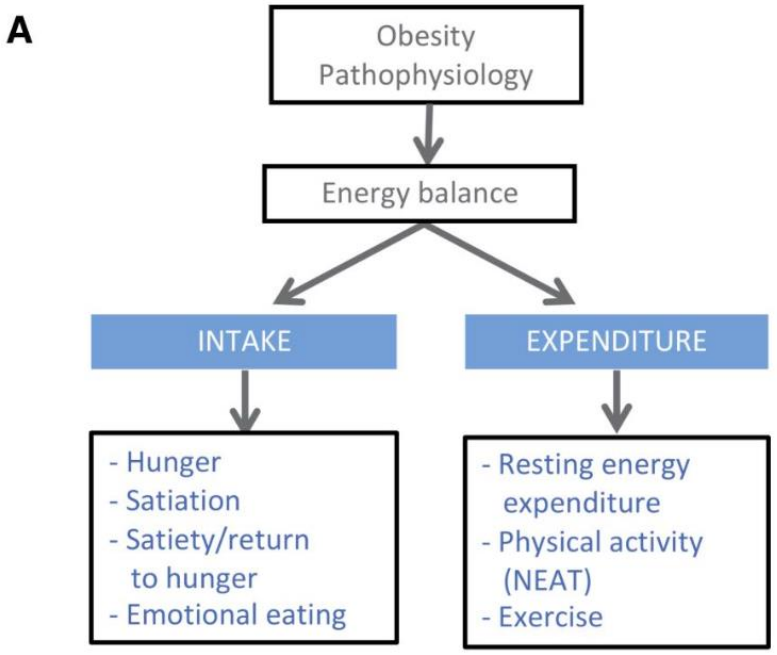


Figure 1 Pathophysiological classification of obesity. (**A**) Illustration of obesity pathophysiology based on energy balance and key components that contribute to human obesity. (**B**) Distribution of participants based on pathophysiological phenotypes in 450 patients with obesity (BMI > 30 kg/m^2). NEAT, nonexercise activity thermogenesis.

Hungry Brain
(Satiation)

Consuming too many calories without feeling full

Hungry Gut
(Satiety)

Feeling hungry shortly after eating

Emotional Hunger
(Reward)

Eating in response to emotional triggers

Slow Burn
(Metabolism)

Burning calories ineffectively

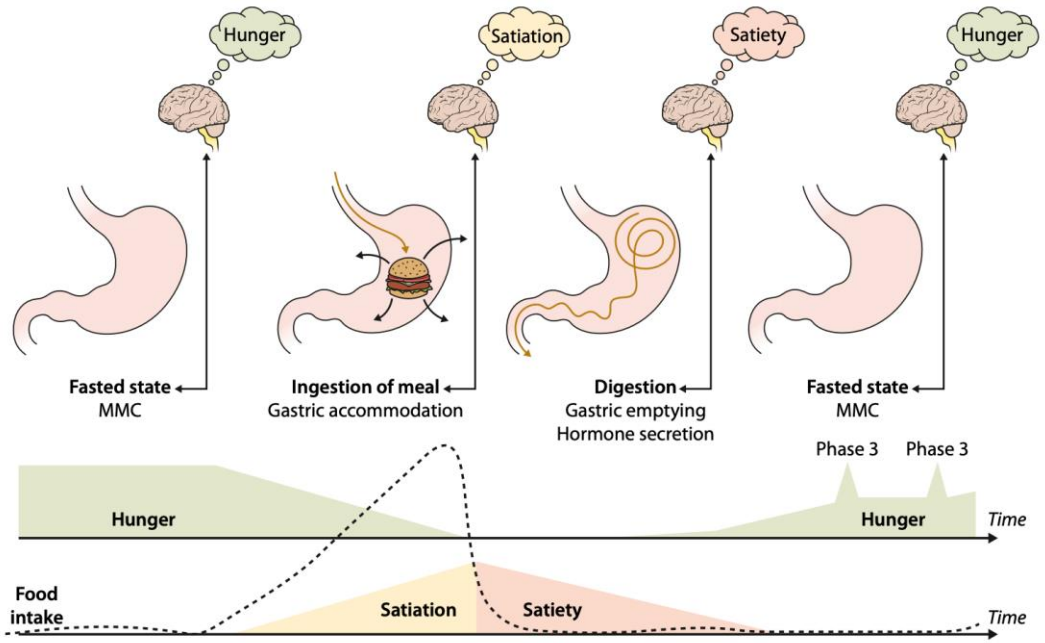


FIGURE 1 Overview of the cycles of hunger and satiation/satiety, with timing relative to the events of food intake and gastrointestinal physiological markers. Hunger is high in the fasting state and decreases as food is ingested, which is paralleled by the rise in satiation. At maximum satiation, meal intake stops, hunger is absent and satiety is at its highest. As satiety drops over time, hunger rises gradually. Gastric emptying is a permissive parameter for return of hunger, but not a main determinant. Peaks of hunger coincide with gastric Phase III of the migrating motor complex

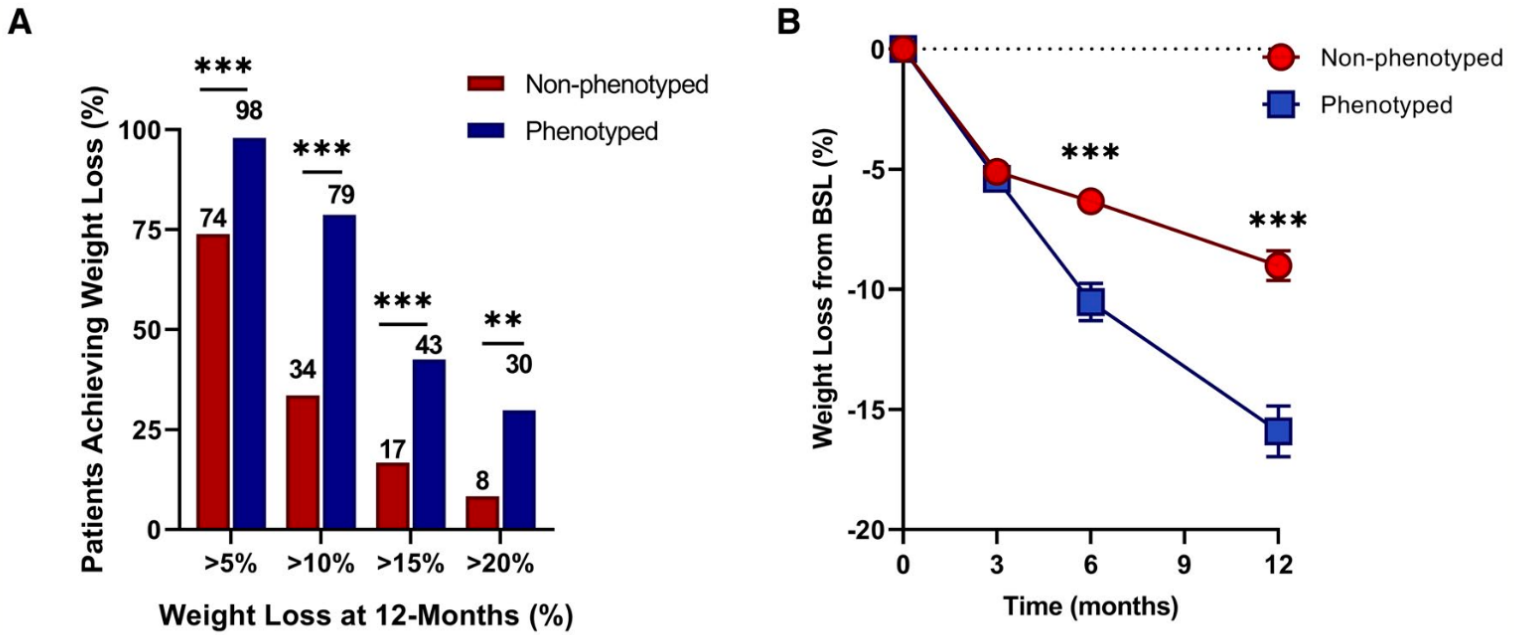
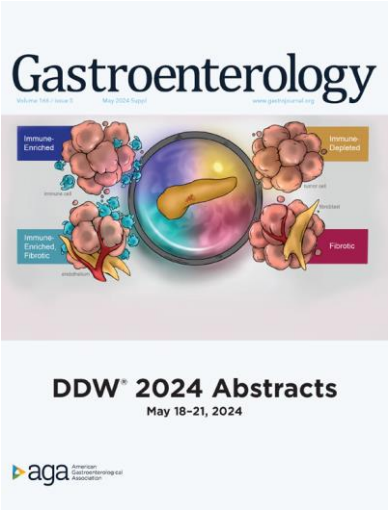


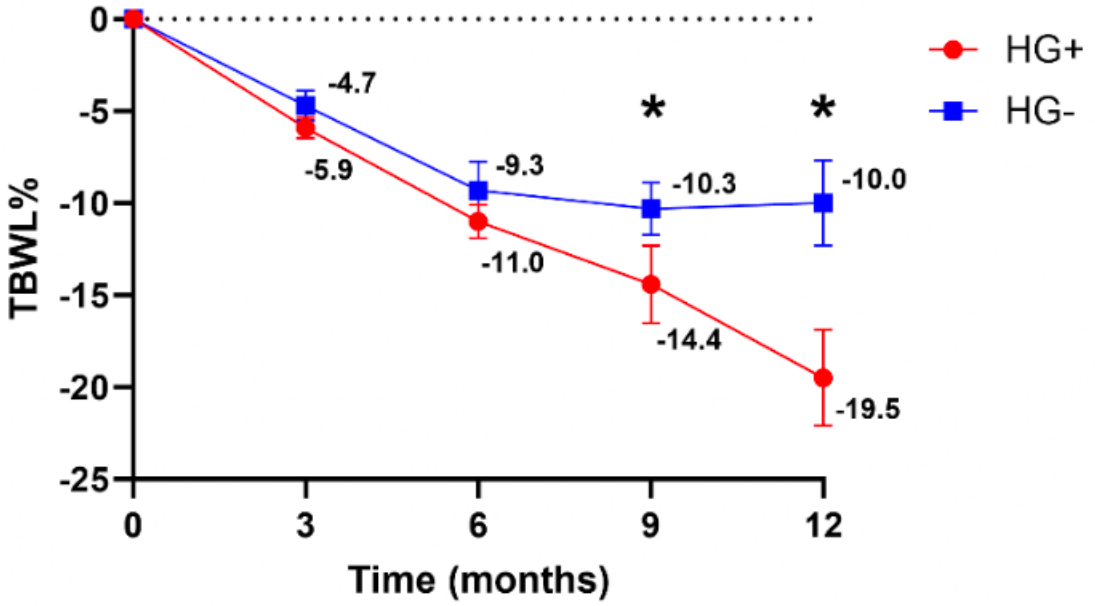
Figure 3 PG pharmacotherapy for obesity management improves weight loss outcomes. (**A**) Percentage of patients achieving levels of weight loss after 1 year of either non-PG ($n = 228$) or PG ($n = 84$) treatment. (**B**) The average percentage of total body weight loss from BSL in non-PG (red circles) and PG (blue squares) treatment at 3, 6, and 12 months. $^{**}P < 0.01$, $^{***}P < 0.001$. BSL, baseline; PG, phenotype guided.



PERFORMANCE OF A MACHINE-LEARNING GENE RISK SCORE BIOMARKER ON PREDICTING RESPONSE TO SEMAGLUTIDE: A PROSPECTIVELY FOLLOWED MULTI-CENTER BIOBANK AND OUTCOMES REGISTRY

Sima Fansa, Elif Tama, Diego Anazco, Lizeth Cifuentes, Wissam Ghusn, Khushboo Gala, Elle Kolkin, Timothy R. O'Connor, Andres Acosta, Maria D. Hurtado

A.



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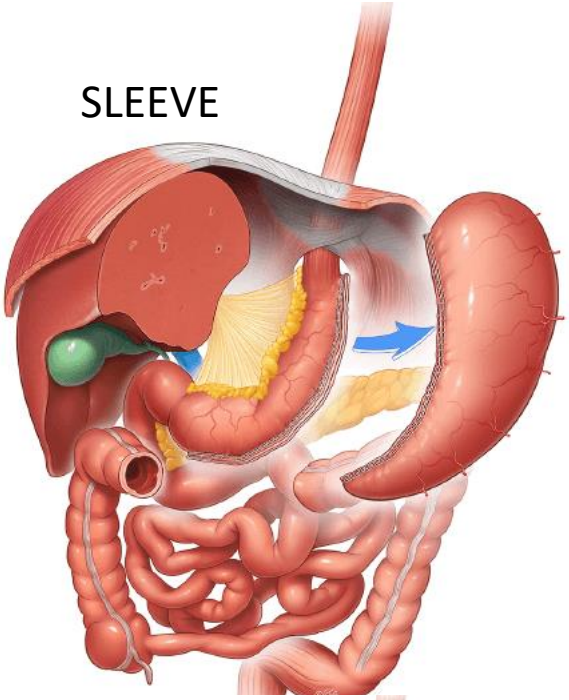
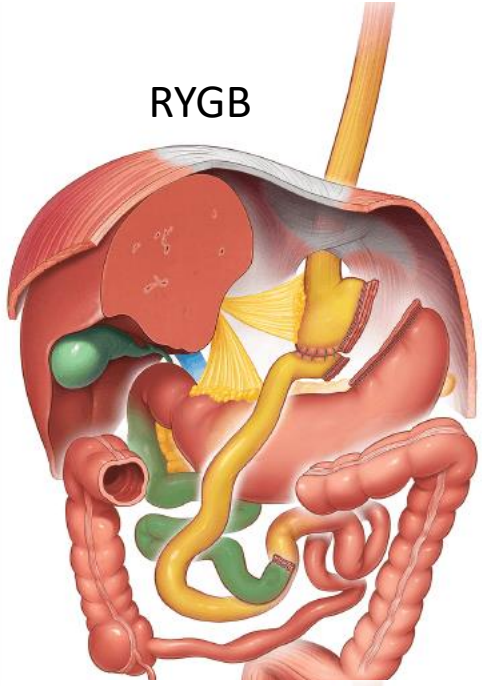
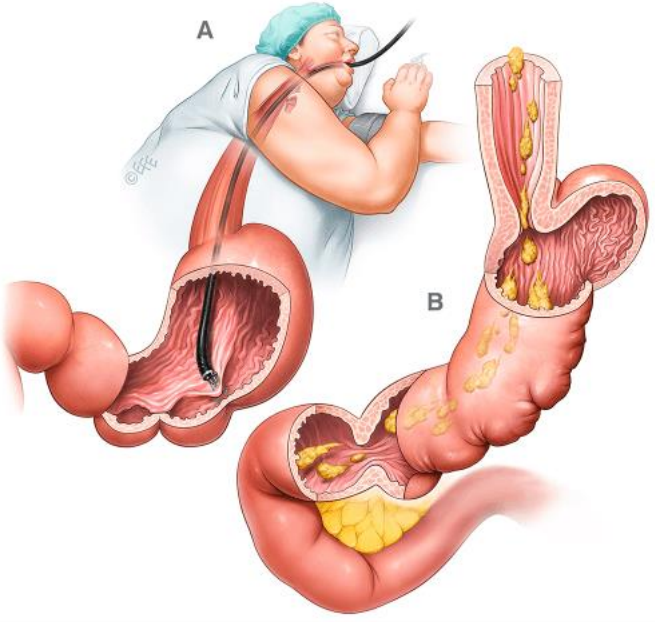
SLEEVE



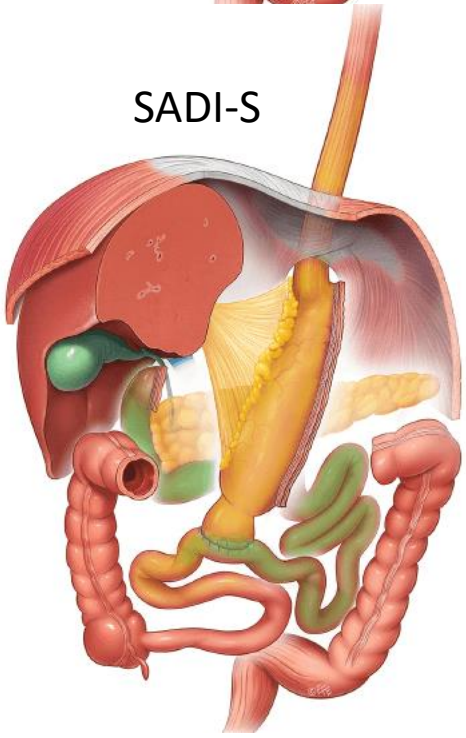
RYGB



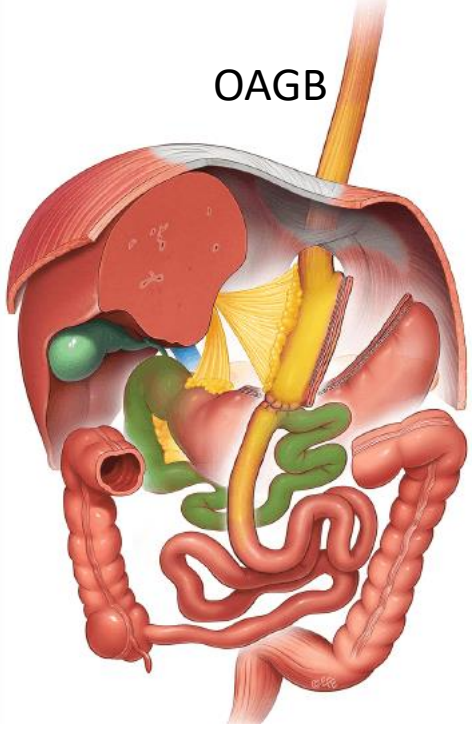
ENDOSLEEVE



SADI-S



OAGB



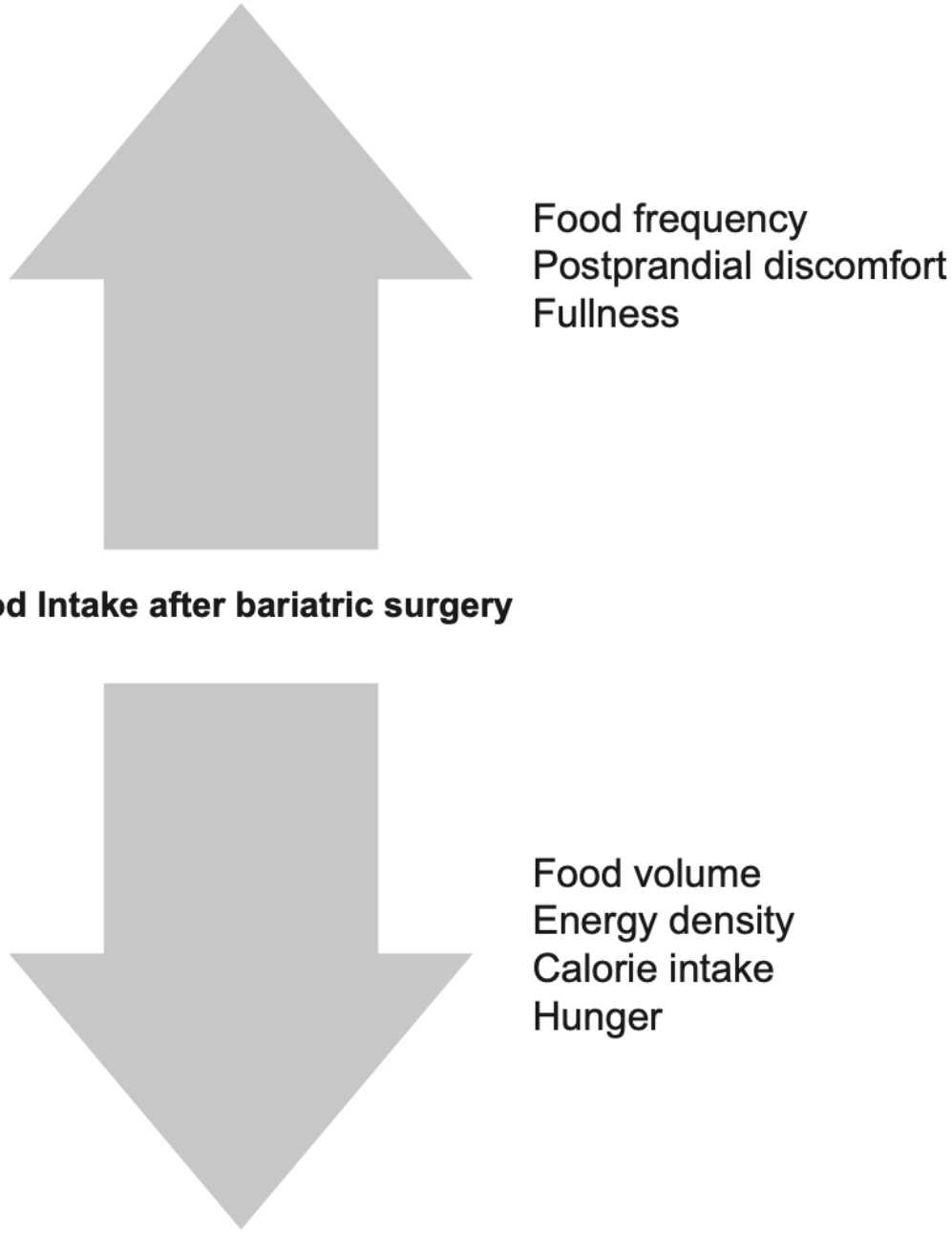
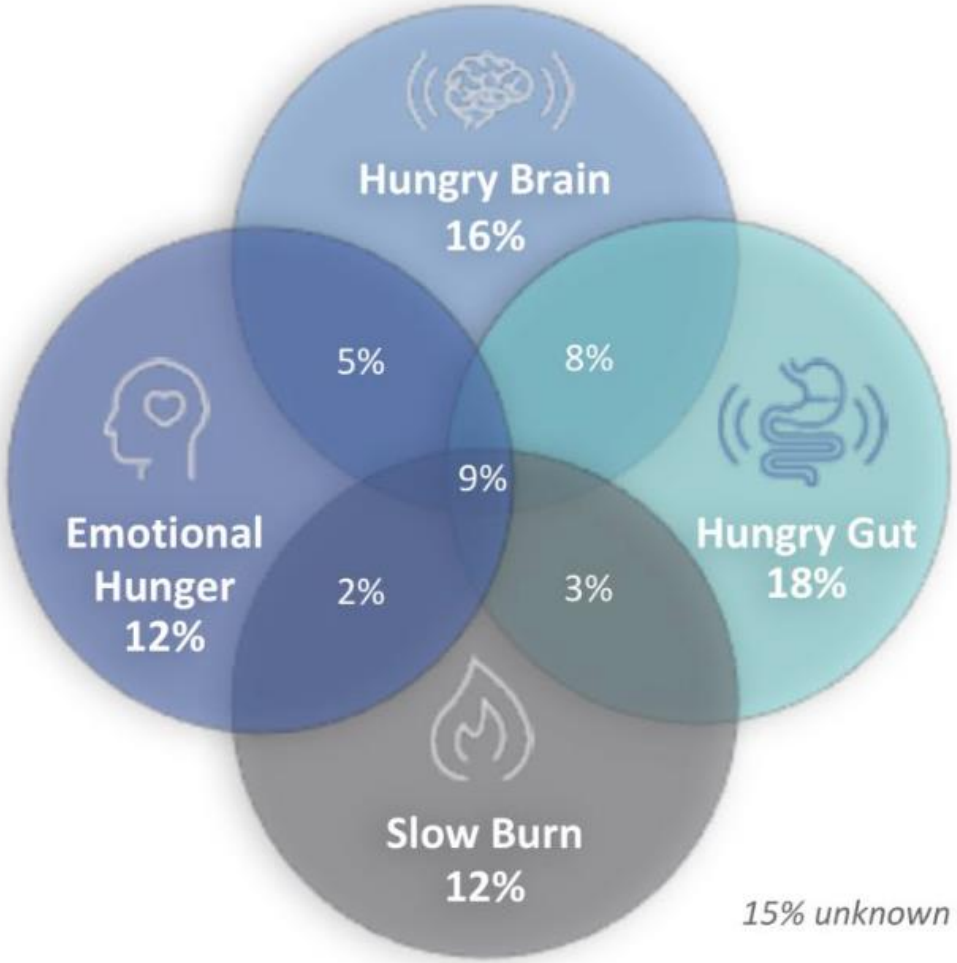


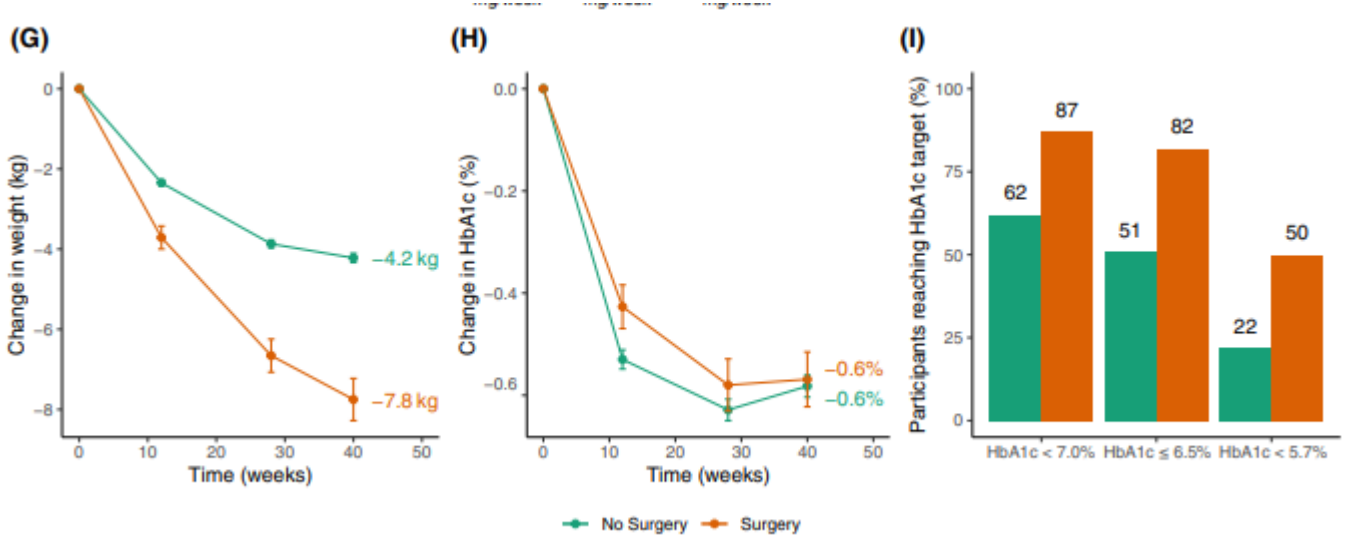
FIGURE 4. Changes in food intake after bariatric surgery.

Obesity category	Phenotype	Test
Food intake–homeostatic	Satiation (hungry brain)	Ad libitum buffet meal, kcal
		VAS–Satisfaction 30 min postprandial, 0-100 mm
	Satiety (hungry gut)	VAS–Fullness 120 min postprandial, 0-100 mm
		Gastric emptying $T_{1/2}$, min
Food intake–hedonic eating	Emotional eating	TEFQ–Emotional Restraint (4-16 scale)
		HADS-A (0-21 scale)
Energy expenditure	Basal metabolic rate	Predicted REE (HB) %
	Nonexercise physical activity	Self-reported steps, #
	Exercise	Self-reported exercise (PASC), 0-8 scale

MULTIDISCIPLINARY TEAM IS THE KEY



TIRZEPATIDE POST CHIRURGIA BARIATRICA



How to cite this article: Buckley A, Suliman S, Allum M, et al. Real world use of tirzepatide in the treatment of type 2 diabetes in an Arab population. *Diabetes Obes Metab.* 2024; 26(8):3381-3391. doi:10.1111/dom.15680

ONE SIZE DOESN'T FIT ALL !

The variability in weight loss response to the current obesity treatment approach is the result of the heterogeneity of this disease's etiology, clinical presentation, and development of associated comorbidities.

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Obesità: fenotipizzazione e risvolti terapeutici
Ferrara, 19 ottobre 2024

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